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AMENDMENTS TO THE SPECIFICATION

In the Specification:

After the material previously added by the Preliminary Amendment on page 78 of the application, please substitute the sequence listing with the substitute sheets (6 pages) attached hereto and renumber the pages with the claims and the abstract accordingly. Please renumber the pages with the claims and the abstract accordingly.

Please replace the paragraph from page 14, line 30, to page 15, line 5, with the following paragraph:

--Figure 23 is a multiple sequence alignment of the ligand binding domains of the human retinoic acid receptor γ (RAR) (SEQ ID NO: 2), the human retinoid X receptor α (RXR- α) (SEQ ID NO: 1), the human progesterone receptor (PR) (SEQ ID NO: 3), the human glucocorticoid receptor (GR) (SEQ ID NO: 4), the human estrogen receptor (ER) (SEQ ID NO: 5) and the NMDA receptor NR1 subunit ($NR1_{011}$) (SEQ ID NO: 6). Conserved identical residues are bold and underlined and similar residues are bold. The triangles (Δ) under the $NR1_{011}$ sequence indicate the five mutation sites in the Penta-mutant. The five mutation sites are R182A, K193A, K202A, R233A, and R252A.--

Please replace the paragraph on page 20 of the Preliminary Amendment (added at page 19, line 18, of the specification) with the following paragraph:

--Figure 45. Sequence alignment of the region that is important for PS potentiation of the NMDAR. PS potentiates the NMDA/glycine response at receptors containing either NR2A (SEQ ID NO: 7) or NR2B (SEQ ID NO: 8) subunits, while it inhibits those containing NR2C (SEQ ID NO: 9) or NR2D (SEQ ID NO: 10). The residues that are different between the two groups (2A/2B and 2C/2D) are highlighted ~~in yellow~~. Residues in the NR2B are mutated to the

amino acids at the corresponding positions in the NR2D.--

Please replace the final paragraph on page 26 of the Preliminary Amendment (added at page 78 of the specification) with the following paragraph:

--Thus, the potentiating effects of PS and spermine are very distinct. PS and spermine modulate the NMDAR via two different routes: spermine modulation is coupled to the gating mechanism through the proton sensor, whereas PS modulation occurs via a route that is independent of the receptor's level of protonation (Figure 41). Because the potentiating effect of sperimine is dependent on the proton sensor, it is plausible that the loss of the spermine effect at NR1a/χ4 containing receptors is not due to a change in the spermine-binding site, but rather a secondary phenomenon that reflects an alteration in proton sensitivity. To investigate this idea, we further characterized NR1a/χ4 receptors to investigate if proton sensitivity is altered in these receptors. (See Figure 41.) The loss of both PS and spermine modulation of the NMMDA/glycine response in receptors containing NR1a/χ4 suggests that these two different routes may converge in a common pathway that modulates the channel gating mechanism. Moreover, the domain we identified at the NR2B subunit (750-839) may be an important structural determinant of this common pathway.--

AMENDMENTS TO THE FIGURES

Please replace Figures 41 and 45 with revised Figures 41 and 45 (enclosed herewith).